solved in pyridine (3 ml.) and after addition of *p*-phenylazobenzoyl chloride (150 mg.) the mixture was kept at 37° for 2 days. The reaction mixture was poured into water, kept for 3 hr., and evaporated. The residue was extracted with chloroform and the extract chromatographed on a column of zinc carbonate.[12] On evaporation of the eluate, a sirup was obtained which crystallized on trituration with ethyl acetate. The crystals were filtered, washed with ethanol and dried, m.p. and mixed m.p. with an authentic specimen of 2,6-di-*O*-methyl-D-glucose 1,3,4-tris-*p*-phenylazobenzoate, 205–207°.[12]

Identification of 2,6-Di-*O*-methyl-D-mannose.—The second component of the mixture of di-*O*-methyl sugars had an R_f value which did not correspond to 2,3-, 2,4-, 3,4-, 3,6- or 4,6-di-*O*-methyl-D-glucose. That it is probably 2,6-di-*O*-methyl-D-mannose is indicated by the fact that when 2,6-di-*O*-methyl-D-glucose was epimerized with alkali[13,24] it gives 2,6-di-*O*-methyl-D-mannose which had the same R_f value as the unknown di-*O*-methyl sugar, and gave the same color on a chromatogram developed with *p*-anisidine. The unknown di-*O*-methyl sugar was readily distinguished by paper chromatography from 2,3- and 3,4-di-*O*-methyl-D-mannose.

The ratio of the methylated sugars was determined in a separate experiment by separation of the components of the hydrolyzate on paper using solvent B, extraction of the appropriate areas of paper, purification of the products by extraction with water, and weighing the residues left after evaporation. The result was tetra-*O*-methyl sugars (1.0 mole), tri-*O*-methyl sugars (11 moles) and di-*O*-methyl sugars (0.93 mole). The corresponding results calculated from the column chromatography are 1:9:1 approx.

Periodate Oxidation of the Glucomannan.—The glucomannan (0.5 g.) was treated with 0.1 *N* sodium metaperiodate (250 ml.) at 5°[25] and the consumption of periodate and the generation of formic acid were determined according to the standard procedures.[26] The molar consumption of periodate per hexose residue was: 0.61 (5 hr.), 0.72 (27 hr.), 0.86 (45 hr.), 0.88 (72 hr.), 0.95 (95 hr.), 1.0 (140 hr.), 1.03 (209 hr., constant value). The number of hexose residues producing 1 mole of formic acid was: 14 (18 hr.), 13.3 (27 hr.), 12.5 (46 hr.), 12.1 (72 hr.), 11.1 (94 hr.), 10.9 (116 hr.), 10.4 (140 hr.).

Reduction of the Periodate-oxidized Glucomannan.—The periodate-oxidized, reaction mixture was neutralized with barium hydroxide and the barium iodate and barium periodate were removed by centrifugation. To the supernatant liquid sodium borohydride (500 mg.) was added and the solution allowed to stand at room temperature for 3 hr. The solution was acidified with acetic acid and evaporated to dryness. The residue was hydrolyzed by heating on the steam-bath for 3 hr. with *N* sulfuric acid. The hydrolyzate was neutralized ($BaCO_3$), filtered, and the solution deionized by passing first through a cation (Amberlite IR 120)[27] and then an anion exchange resin (Duolite A_4).[28] The resulting solution was evaporated to a sirup which, upon chromatographic analysis using butan-1-ol–ethanol–water (4:1:5)[20] and ammoniacal silver nitrate spray, was found to contain D-glucose, D-mannose, glyceritol and erythritol. The monosaccharides were determined by the phenol–sulfuric acid method[21] and the polyhydric alcohols[29] by oxidation with periodate[16] followed by the determination of formaldehyde with chromotropic acid.[30] The ratios of the components in the hydrolyzate were: D-glucose (1.8 moles), D-mannose (0.7 mole), glyceritol (1.0 mole) and erythritol (14.8 moles).

(24) M. L. Wolfrom and W. L. Lewis, THIS JOURNAL, **50**, 837 (1928).
(25) M. Abdel-Akher and F. Smith, *ibid.*, **73**, 994 (1951).
(26) P. Fleury and J. Lange, *J. pharm. chim.*, [8] **17**, 107 (1933).
(27) A product of the Rohm and Haas Co., Philadelphia, Pa.
(28) A product of the Chemical Process Co., Redwood City, Calif.
(29) J. R. Hamilton and F. Smith, THIS JOURNAL, **78**, 5910 (1956).
(30) M. Lambert and A. C. Neish, *Can. J. Res.*, **B28**, 83 (1950).

ST. PAUL, MINN.

[CONTRIBUTION FROM THE DEPARTMENT OF AGRICULTURAL BIOCHEMISTRY, UNIVERSITY OF MINNESOTA]

Oxidation of Glycogen with Periodic Acid[1]

BY M. ABDEL-AKHER AND F. SMITH

RECEIVED OCTOBER 10, 1958

The periodate oxidation product of glycogen, glycogen polyaldehyde, is isolated in 97% yield by a simple freezing method. The course of the periodate oxidation of glycogen was investigated and the structure of the polyaldehyde discussed.

In extending our investigations into the reduction products of periodate oxidized glycosides[2,3] to polysaccharides[4] it was necessary to obtain the intermediate glycogen polyaldehyde in a pure form for structural studies. Unlike starch, which reacts with periodic acid to give a polyaldehyde that is insoluble in cold water,[5] the glycogen polyaldehyde like the original polysaccharide remains dissolved in the reaction mixture. It is shown herein, however, that if the reaction mixture is frozen overnight at −5 to −10° and allowed to thaw at room temperature the glycogen polyaldehyde remains as a cold-water insoluble, flocculent precipitate, which may be washed with water to remove inorganic impurities. Other methods such as dialysis and ion exchange resins were used but they were inferior to this freezing technique.

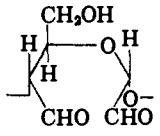
The polyaldehyde from different samples of glycogen showed very similar properties; the material is a white, amorphous powder which is insoluble in water and the usual solvents, but soluble in warm, aqueous potassium or sodium acetate giving solutions having $[\alpha]_D$ +20°. The polyaldehyde reduced Fehling solution strongly, gave a deep blue color with the Molisch reagent and showed a positive Schiff test; unlike the parent polysaccharide, however, it gave no color with iodine.

The polyaldehyde was sensitive to both acid and alkali. Upon hydrolysis with mineral acid, the polyaldehyde underwent decomposition and a brown precipitate was produced; glucose was detected by paper chromatography in the hydrolyzate. Heating the polyaldehyde with a solution of sodium hydroxide also caused decomposition.

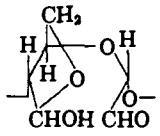
In a discussion of the structure of the starch polyaldehyde,[6] it was pointed out that the eryth-

(1) The experimental part of this paper forms part of a thesis submitted by M.A-A. to the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Ph.D., 1952; paper No. 3916 Scientific Journal Series, Minnesota Agricultural Experiment Station.
(2) M. Abdel-Akher, J. E. Cadotte, R. Montgomery, F. Smith, J. W. Van Cleve and Bertha A. Lewis, *Nature*, **171**, 474 (1953).
(3) F. Smith and J. W. Van Cleve, THIS JOURNAL, **77**, 309 (1955).
(4) M. Abdel-Akher, J. K. Hamilton, R. Montgomery and F. Smith, *ibid.*, **74**, 4970 (1952).
(5) E. L. Jackson and C. S. Hudson, *ibid.*, **59**, 2049 (1937).
(6) J. H. Mitchell and C. B. Purves, *ibid.*, **64**, 589 (1942).

rose residue in I formed by periodate cleavage of a 1,4-linked glucose residue might well exist in a furanose ring form (II).

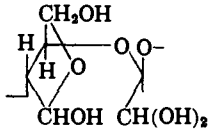


I

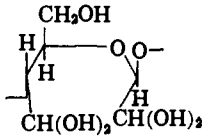


II

The above structure, however, does not satisfy the analysis of the glycogen polyaldehyde which was too low in carbon and too high in hydrogen for I and II. It is possible that partial hydration of the aldehydic groups takes place, a view suggested[7] to explain the structure of cellulose polyaldehyde. These authors showed by infrared studies that free aldehydic groups are absent in the cellulose polyaldehyde and suggested partial hydration and cyclization as in III or complete hydration of the aldehydic groups as in IV. Cited in support of

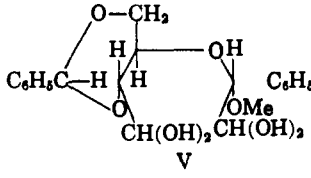


III

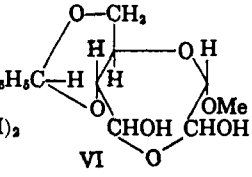


IV

this view was the report[7] that the so-called dialdehyde, prepared by periodate oxidation of methyl 4,6-*O*-benzylidene-α-D-glucoside, existed as the dihydrate V. It has been shown[8] recently, however, that this so-called dialdehyde dihydrate

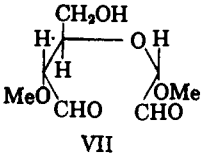


V

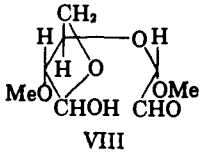


VI

contains one molecule of water of crystallization and one molecule of water of constitution,[9,10] the latter being involved in the mutual union of the two aldehydic groups to give the dioxane structure VI. Pertinent to the discussion is the observation[8] that the so-called dialdehyde VII from 4-*O*-methyl-α-D-glucopyranoside probably exists in the cyclic acetal form VIII.

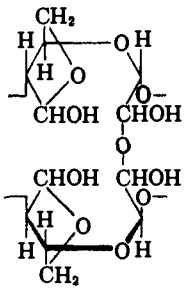


VII

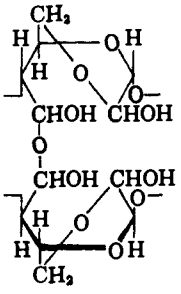


VIII

The analysis of the so-called glycogen polyaldehyde shows that approximately one molecule of water is shared between two aldehydic groups as in the two structures IX and X.



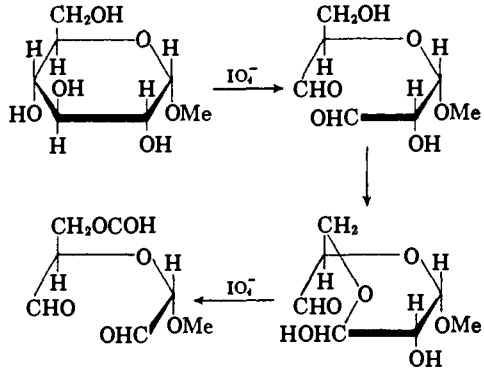
IX



X

That this general type of structure is most probably correct is supported by the recent observation[11] that treatment of amylopectin polyaldehyde with methanolic hydrogen chloride introduces methyl acetal groups with concomitant cross-linking similar to that depicted in IX and X.

The periodate oxidation of glycogen was found to differ from that of the simple glycosides. In the case of methyl α-D-glucoside and methyl β-maltoside the periodate consumption proceeds rapidly to completion according to theory; the formic acid was produced much more slowly, the theoretical yield being reached long after periodate uptake was complete. The slow development of formic acid clearly indicates that while carbon–carbon bonds are cleaved with the periodate, the formic acid remains attached to the cleaved molecule. These results could be explained by the formation of an intermediate lactol which is subsequently oxidized by the periodate to form an ester of formic acid, a view previously suggested.[12,13] This view implies a stepwise oxidation where the first oxidation product forms an internal (or possibly an external) lactol. The lactol is oxidized in the second step by the periodate to give an ester of formic acid instead of free formic acid. The ester, on standing in cold water, undergoes slow hydrolysis with the liberation of formic acid thus



In the case of glycogen the periodate oxidation took a somewhat different course from that with methyl α-D-glucoside and with methyl β-maltoside. for although the slow development of formic acid was similar to that shown by the glycosides, the periodate consumption proceeded rapidly at the beginning, then slowed down, and reached com-

(7) J. W. Rowen, Florence H. Forziati and R. E. Reeves, THIS JOURNAL, **73**, 4484 (1951).

(8) I. J. Goldstein, Bertha A. Lewis and F. Smith, *Chemistry & Industry*, 595 (1958).

(9) *Cf.* W. D. Maclay, R. M. Hann and C. S. Hudson, THIS JOURNAL, **61**, 1660 (1939).

(10) I. J. Goldstein, Bertha A. Lewis and F. Smith, *ibid.*, **80**, 939 (1958).

(11) I. J. Goldstein and F. Smith, *Chemistry & Industry*, 40 (1958).

(12) R. C. Hockett and W. S. McClenahan, THIS JOURNAL, **61**, 1667 (1939).

(13) T. G. Halsall, E. L. Hirst and J. K. N. Jones, *J. Chem. Soc.*, 1427 (1947).

pletion a long time after the theoretical amount of formic acid had been produced. It seems likely that the terminal non-reducing ends in the glycogen molecule, which produce formic acid in this reaction, are exposed and easily reached by the reagent so that they undergo oxidation in the same way as methyl α-D-glucopyranoside. On the other hand, the innermost glucose residues are not exposed so that they are oxidized more slowly and, consequently, the periodate consumption lags behind the formic acid production.

Experimental

Periodate Oxidation of Glycogen.—To a solution of horse liver glycogen (5.332 g.) in water (250 ml.), *N* periodic acid (200 ml.) was added, and the volume was adjusted to 500 ml. by the addition of water. The oxidation was allowed to proceed at 5–6° in the dark. After three weeks, the glycogen had consumed[14] one mole of periodate per glucose residue and no further change occurred after keeping for another week.

Isolation of the Glycogen Polyaldehyde. (1) By Freezing. After 4 weeks, the above periodate oxidation reaction mixture (450 ml.) was allowed to freeze overnight at −10°. The frozen reaction mixture was allowed to thaw at room temperature when the oxidation product, glycogen polyaldehyde, separated as a white solid. The polyaldehyde was centrifuged, washed several times with cold water until free from iodate and periodate (tested with acidified potassium iodide), then with ethanol, acetone, diethyl ether, and finally dried *in vacuo* at 90–95° for 1–2 hr. The yield of white amorphous material was 4.05 g.

(2) By the Use of Exchange Resins.—Glycogen (3 g.) from horse liver was oxidized with periodic acid as in (1) above. After 4 weeks, ethylene glycol was added to destroy the excess periodic acid and this was followed by treatment with (Duolite A4[15]) anion exchange resin in order to obtain a neutral solution free from iodate. The neutral solution was evaporated to dryness under reduced pressure (bath 50–60°), ethanol being added to facilitate the final drying *in vacuo*. The product was a horny-like material which was insoluble in water.

(3) By Dialysis.—After the oxidation of glycogen was completed as described before, the reaction mixture was dialyzed against distilled water for 5–6 days and evaporated to dryness *in vacuo*. This method likewise gave a horny-like product as in (2) above.

Properties of Glycogen Polyaldehyde. (1) General Properties.—The glycogen polyaldehyde, prepared from different samples of glycogen by the freezing method, is a white solid which is insoluble in water and the usual solvents; it dissolves on warming in dilute (5–10%) aqueous potassium or sodium acetate. It strongly reduces Fehling solution and shows a deep blue ring with the Molisch reagent. Addition of Schiff reagent to a suspension of the glycogen polyaldehyde in water renders the suspended material violet, but the aqueous layer remains colorless. It would thus appear that the polyaldehyde is completely insoluble in water. The polyaldehyde gave no color with iodine.

(2) Optical Rotation.—The optical rotation was determined in the following way: Glycogen polyaldehyde (100 mg.), dried *in vacuo* at 90–95°, was transferred to a 10-ml. volumetric flask, followed by 10% aqueous potassium acetate (7 ml.). The flask was immersed in boiling water (5 min.) to allow the material to dissolve, cooled, and adjusted to volume by adding 10% aqueous potassium acetate.

The specific optical rotations of glycogen polyaldehydes prepared from different samples of glycogen are shown in Table I.

(3) Chemical Analysis.—The elementary analysis of glycogen polyaldehyde from four different sources is recorded in Table II.

(4) Hydrolysis with Dilute Mineral Acid.—Glycogen polyaldehyde (0.4345 g.) was heated (sealed tube) with 0.1 *N* sulfuric acid (5 ml.) in boiling water for 3.5 hr. during which time the material dissolved and the color of the hydrolyzate changed first to yellow followed by brown, and then dark brown at which stage a dark brown material separated. The hydrolyzate was neutralized with Duolite A4 anion exchange resin, filtered and concentrated to a small volume. Chromatographic analysis on paper, using phenol saturated with water as the irrigating solvent, showed that glucose was present. The significance of this finding will be discussed later; *cf.* ref. 4.

TABLE I

SPECIFIC ROTATION OF GLYCOGEN POLYALDEHYDE IN AQUEOUS POTASSIUM ACETATE

Source of glycogen polyaldehyde	$[\alpha]^{25}D$
Horse liver glycogen	+20.3°
Ox liver glycogen	+20.8
Rat liver glycogen	+20.8
Crappie (*Pomoxis annularis*) fish liver glycogen	+20.8
Rabbit liver glycogen	+20.3
Walleyed pike (*Stizostedion vitreum*) fish liver glycogen	+20.8
Turkey liver glycogen	+20.4
Bee larvae glycogen	+21.1

TABLE II

Source of glycogen polyaldehyde	Carbon, %[a]	Hydrogen, %
Ox liver glycogen	41.16	5.76
Crappie fish liver glycogen	41.74	5.90
Normal rabbit liver glycogen	42.28	5.62
Turkey liver glycogen	41.50	5.94

[a] Calcd. for $C_6H_8O_5$: C, 44.84; H, 5.2. For $(C_6H_8O_5)_2 \cdot H_2O$: C, 42.6; H, 5.3. For $(C_6H_8O_5)_4 \cdot 3H_2O$: C, 41.5; H, 5.5.

(5) The Effect of Alkali.—Glycogen polyaldehyde (0.1 g.) was treated with *N* sodium hydroxide (15 ml.). After shaking for a few minutes, the compound dissolved to give a solution which was strongly reducing to Fehling solution and gave a deep blue ring with Molisch reagent. The solution was warmed on a steam-bath for about 20 min. during which time it became dark brown in color. The brown solution was decolorized with charcoal giving a faint yellow solution which was non-reducing to Fehling reagent. The tryptophan–sulfuric acid test for glyoxylic acid was negative.

Comparison of the Rate of the Consumption of Periodate with the Production of Formic Acid during the Oxidation of Certain Carbohydrates with Sodium Periodate. (1) Methyl α-D-Glucopyranoside.—To a solution of methyl α-D-glucopyranoside (0.0814 g., m.p. 165–166°, $[\alpha]^{18}D$ +158.7° in water (*c* 2.6)) in water (100 ml. approx.), was added 0.2857 *N* sodium metaperiodate (25 ml.) and the volume adjusted to 200 ml. by addition of water after which the reaction mixture was kept at 5–6° in the dark.[11] A blank experiment was carried out at the same time under the same conditions. Aliquots (10 ml.) were withdrawn at the indicated intervals. One aliquot was used for the determination of formic acid by direct titration with barium hydroxide solution and another aliquot was used for the determination of the periodate consumption, using the usual sodium arsenite method.[16]

The consumption of periodate and the production of formic acid represented as a percentage of theory were: periodate consumption: 89% (after 1.5 hr.), 95.5% (2.5 hr.), 99% (7 hr.), 101% (10 hr., constant for further 80 hr.); formic acid production: 40% (1.5 hr.), 57% (7 hr.), 65% (10 hr.), 82% (26 hr.), 99.2% (66 hr., constant for further 22 hr.).

(2) Methyl β-Maltoside.—To a solution of methyl β-maltoside monohydrate (0.1636 g., m.p. 111–113°, $[\alpha]^{20}D$ +84.7° in water (*c* 1.57)) in water (100 ml.), was added 0.2856 *N* sodium metaperiodate (25 ml.); the volume was adjusted to 250 ml. with water and the reaction was carried out as in (1). The periodate consumption and the formic acid production as a percentage of the theory were: periodate consumption: 81% (2.5 hr.), 82% (3.5 hr.), 88% (7.5 hr.), 103% (24 hr., constant for further 114 hr.); formic acid production: 37% (3.5 hr.), 44% (7.5 hr.), 57% (24 hr.), 75% (52 hr.), 96.5% (90 hr., constant for further 48 hr.).

(3) Glycogen.—To a solution of ox liver glycogen (1.0275 g.) in water (100 ml.) was added 0.2856 *N* sodium meta-

(14) M. Abdel-Akher and F. Smith, THIS JOURNAL, **73**, 994 (1951).

(15) A product of the Chemical Process Co., Redwood City, Calif.

(16) P. Fleury and J. Lange, *J. pharm. chim.*, **17**, 107 (1933).

periodate (75 ml.) and the volume was adjusted to 500 ml. by addition of water. Periodate consumption and formic acid production determined as before were: periodate consumption: 82% (21 hr.), 91% (41 hr.), 96% (64 hr.), 97% (112 hr.), 99% (7 days), 103% (16 days), 104% (22 days, constant for further 4 days); formic acid production: 67% (21 hr.), 83% (41 hr.), 89.5% (64 hr.), 96% (88 hr.), 100% (112 hr., constant for further 10 days). The theoretical values were calculated on the basis of 13 glucose residues per average repeating unit which consume 14 moles of periodate and liberate 1 mole of formic acid.

Acknowledgments.—The authors thank the Corn Industries Research Foundation for financial support and M.A.A. thanks the University of Cairo, Egypt, for a scholarship.

ST. PAUL, MINN.

[CONTRIBUTION FROM THE STERLING-WINTHROP RESEARCH INSTITUTE AND RENSSELAER POLYTECHNIC INSTITUTE]

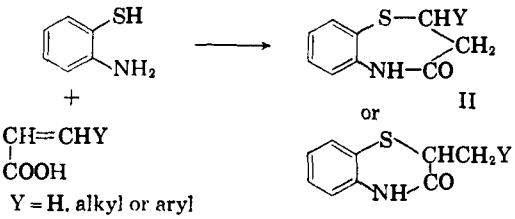
A New Synthesis of Some 2-Substituted-3,4-dihydro-3-oxo-1,4,2-benzothiazine Derivatives

BY FRED. K. KIRCHNER[1] AND E. JOHN ALEXANDER[2]

RECEIVED JULY 29, 1958

It has been found that β-benzoylacrylic acids, maleamic acids, maleanilic acids and maleic acid monophenylhydrazides condense with 2-aminobenzenethiol to form six- rather than seven-membered heterocyclic rings in a manner analogous to maleic acid.

Mills and Whitworth[3] reported that 2-aminobenzenethiol reacted with simple α,β-unsaturated acids (Ia) to produce 4-oxo-2,3,4,5-tetrahydro-1,5-benzothiazepines (II). However, treatment of 2-aminobenzenethiol with maleic acid resulted in the formation of 3,4-dihydro-3-oxo-1,4,2-benzothiazine-2-acetic acid (IIIa).[3]



Ia, Y = H, alkyl or aryl
Ib, Y = COAr
Ic, Y = CONRR'
Id, Y = CONRAr
Ie, Y = CONHNHAr

IIIa, Y = COOH
IIIb, Y = COAr
IIIc, Y = $CONHC_6H_5$

The present investigation was undertaken to determine the structure of the products formed when 2-aminobenzenethiol reacted with more complex α,β-unsaturated acids, *e.g.*, β-benzoylacrylic acids (Ib),[4-6] maleamic acids (Ic),[7] maleanilic acids (Id)[8] and maleic acid monophenylhydrazides (Ie).[9]

We have found, that when 2-aminobenzenethiol reacted with a β-benzoylacrylic acid (Ib), 3,4-dihydro-3-oxo-2-phenacyl-1,4,2-benzothiazine derivatives (IIIb, Table I) could be isolated in good yield. With the exception of compounds 7, 9, 10, 12 and 13, all of the compounds in Table I were prepared by a general technique (see Experimental part).

The 2-(4'-aminophenacyl) derivative (no. 7), which was prepared from the acetamido compound (no. 8), was acylated with butyric (no. 9) and hexanoic anhydride (no. 10). Compounds 12 and 13 were prepared by the reduction of the adducts formed from 4-chloro-2-nitrobenzenethiol[10] and the corresponding β-benzoylacrylic acid derivative.

The oxime was the only ketone derivative of 3,4-dihydro-3-oxo-2-phenacyl-1,4,2-benzothiazine that could be prepared. This was converted by a Beckmann rearrangement to 3,4-dihydro-3-oxo-1,4,2-benzothiazine-2-acetanilide (IIIc, no. 42) which was also formed directly from the acid IIIa and by the condensation of maleanilic acid (no. 25) and 2-aminobenzenethiol. This fact, coupled with the observations that the phenacyl derivative (no. 1) could be prepared alternatively from α-chloro-β-benzoylpropionic acid[11] and that compound 1 failed to acetylate when boiled with acetic anhydride,[12] substantiated the inference that 3,4-dihydro-3-oxo-2-phenacyl-1,4,2-benzothiazines were formed from the condensation of β-benzoylacrylic acids and 2-aminobenzenethiol.

When maleamic acids[7] (Ic, Table II), maleanilic acids[8] (Id, Table II), or maleic acid monophenylhydrazides[9] (Ie, Table IV) were treated with 2-aminobenzenethiol the condensation products[13] were easily isolated. This synthesis was also carried out by mixing an amine, aniline or phenylhydrazine derivative with maleic anhydride in pyridine and then adding 2-aminobenzenethiol. The fact that the condensation products were amides (Table III), anilides (Table III) and phenylhydrazides (Table

(1) Adjunct Professor, Rensselaer Polytechnic Institute.

(2) This paper is based on a thesis submitted by E. John Alexander to the Graduate School of Rensselaer Polytechnic Institute in partial fulfillment of the requirements for the degree of Doctor of Philosophy, May, 1956.

(3) W. H. Mills and J. B. Whitworth, *J. Chem. Soc.*, **130**, 2738 (1927).

(4) D. Papa, E. Schwenk, F. Villani and E. Klingsberg, THIS JOURNAL, **70**, 3356 (1948).

(5) B. J. Cramer, W. Schroeder, W. J. Moran, C. H. Nield, M. Edwards, C. I. Jarowski and B. Puetzer, *J. Am. Pharm. Assoc.*, **37**, 439 (1948).

(6) F. K. Kirchner, J. H. Bailey and C. J. Cavallito, THIS JOURNAL, **71**, 1210 (1949).

(7) C. A. Sears and D. J. Wilson, U. S. Patent 2,723,991 (1955); *C. A.*, **50**, 13992a (1956).

(8) C. D. Hurd, A. S. Roe and J. W. Williams, *J. Org. Chem.*, **2**, 314 (1938).

(9) J. Druey, A. Hüni, K. Meier, B. H. Ringler and A. Staheiln, *Helv. Chim. Acta*, **37**, 510 (1954).

(10) K. Brand and A. Wirsing, *Ber.*, **46**, 820 (1913).

(11) J. Bougault and P. Charbrier, *Compt. rend.*, **224**, 656 (1947).

(12) Mills and Whitworth have shown (ref. 3) that 4-oxo-2,3,4,5-tetrahydro-1,5-benzothiazepines readily acetylated in the 5-position under these conditions.

(13) The nature of by-products produced during these condensations is still undergoing investigation, the results of which will be reported at a later date.